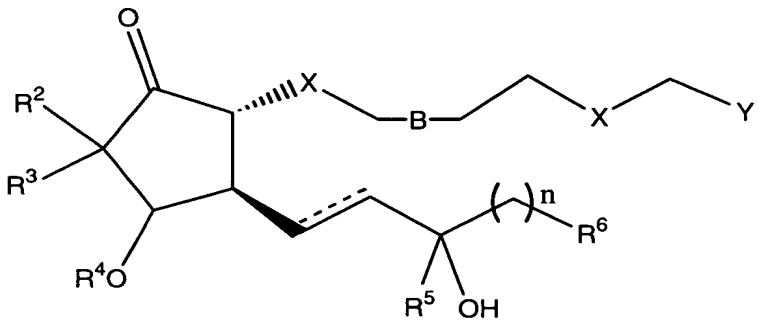
CLAIMS

What is claimed is:

1. A method of treating ocular hypertension or glaucoma which comprises administering to an animal having ocular hypertension or glaucoma a therapeutically effective amount of a compound represented by the general Formula I:



Formula I

wherein the dashed lines indicate the presence or absence of a bond, the hatched wedges indicate the α (down) configuration, and the solid triangles indicate the β (up) configuration;

B is a single, double, or triple covalent bond;

n is 0-6;

X is CH_2, S or O;

Y is $CONHCH_2CH_2OH$ or $CON(CH_2CH_2OH)_2$,

R is H, C_{1-6} alkyl or C_{2-6} alkenyl;

R^2 and R^3 are C_{1-6} linear alkyl which may be the same or different, and may be bonded to each other such that they form a ring incorporating the carbon to which they are commonly attached;

R^4 is hydrogen, R, C(=O)R, or any group that is easily removed under physiological conditions such that R^4 is effectively hydrogen;

R^5 is hydrogen or R; and

R^6 is

i) hydrogen;

ii) a linear or branched hydrocarbon containing between 1 and 8 carbon atoms, which may contain one or more double or triple bonds, or oxygen or halogen derivatives of said hydrocarbon, wherein 1-3 carbon or hydrogen atoms may be substituted by O or a halogen; or

iii) aryloxy, heteroaryloxy, C_{3-8} cycloalkyloxy, C_{3-8} cycloalkyl, C_{6-10} aryl or C_{3-10} heteroaryl, wherein one or more carbons is substituted with N, O, or S; and which may contain one or more substituents selected from the group consisting of halogen, trihalomethyl, cyano, nitro, amino, hydroxy, C_{6-10} aryl, C_{3-10} heteroaryl, aryloxy, heteroaryloxy, C_{1-6} alkyl, OR, SR, and SO_2R.

2. A method of treating ocular hypertension or glaucoma which comprises administering to an animal having ocular hypertension or glaucoma a therapeutically effective amount of a compound selected from the group consisting of

(3-{(1*R*,4*S*,5*S*)-5-(3-chloro-benzo[b]thiophen-2-yl)-3-hydroxy-pent-1-enyl]-4-hydroxy-3,3-dimethyl-2-oxo-cyclopentylsulfanyl}-propylsulfanyl)-acetic acid methyl ester (**21, 22**);

(3-{(1*R*,4*S*,5*S*)-5-(3-chloro-benzo[b]thiophen-2-yl)-3-hydroxy-pent-1-enyl]-4-hydroxy-3,3-dimethyl-2-oxo-cyclopentylsulfanyl}-propylsulfanyl)-acetic acid (**23, 24**);

(*Z*)-7-{(1*R*,4*S*,5*R*)-5-[(*E*)-5-(3-chloro-benzo[b]thiophene-2-yl)-3-hydroxy-pent-1-enyl]-4-hydroxy-3,3-dimethyl-2-oxo-cyclopentyl}-hept-5-ynoic acid methyl ester (**34, 35**);

(*Z*)-7-{(1*R*,4*S*,5*R*)-5-[(*E*)-5-(3-chloro-benzo[b]thiophene-2-yl)-3-hydroxy-pent-1-enyl]-4-hydroxy-3,3-dimethyl-2-oxo-cyclopentyl}-hept-5-ynoic acid (**36,37**);

(*Z*)-7-{(1*R*,4*S*,5*R*)-5-[(*E*)-5-(3-chloro-benzo[b]thiophene-2-yl)-3-hydroxy-pent-1-enyl]-4-hydroxy-3,3-dimethyl-2-oxo-cyclopentyl}-hept-5-enoic acid methyl ester (**38,39**);

(*Z*)-7-{(1*R*,4*S*,5*R*)-5-[(*E*)-5-(3-chloro-benzo[b]thiophene-2-yl)-3-hydroxy-pent-1-enyl]-4-hydroxy-3,3-dimethyl-2-oxo-cyclopentyl}-hept-5-enoic acid (**40,41**);

(Z)-7-[(1R,4S,5R)-4-Hydroxy-5-((E)-3-hydroxy-5-phenyl-pent-1-enyl)-3,3-dimethyl-2-oxo-cyclopentyl]-hept-5-enoic acid methyl ester (**50,51**)

(Z)-7-[(1R,4S,5R)-4-Hydroxy-5-((E)-3-hydroxy-5-phenyl-pent-1-enyl)-3,3-dimethyl-2-oxo-cyclopentyl]-hept-5-enoic acid (**52,53**)

(*Z*)-7-[(1*R*,4*S*,5*R*)-5-((*E*)-4-Benzo[b]thiophen-2-yl-3-hydroxy-but-1-enyl)-4-hydroxy-3,3-dimethyl-2-oxo-cyclopentyl]-hept-5-enoic acid (**54,55**)

7-[(1*R*,4*S*,5*R*)-5-((*E*)-4-Benzo[b]thiophen-2-yl-3-hydroxy-but-1-enyl)-4-hydroxy-3,3-dimethyl-2-oxo-cyclopentyl]-heptanoic acid (**56,57**)

(*Z*)-7-[(1*R*,4*S*,5*R*)-5-(4-Benzo[b]thiophen-2-yl-3-hydroxy-butyl)-4-hydroxy-3,3-dimethyl-2-oxo-cyclopentyl]-hept-5-enoic acid (**58,59**)

(*Z*)-7-[(1*R*,4*S*,5*R*)-5-((*E*)-4-Benzo[b]thiophen-2-yl-3-hydroxy-but-1-enyl)-4-hydroxy-3,3-dimethyl-2-oxo-cyclopentyl]-hept-5-enoic acid ethylamide (**60,61**)

(*Z*)-7-[(1*R*,4*S*,5*R*)-5-((*E*)-4-Benzo[b]thiophen-2-yl-3-hydroxy-but-1-enyl)-4-hydroxy-3,3-dimethyl-2-oxo-cyclopentyl]-hept-5-enoic acid diethylamide (**62,63**)

(*Z*)-7-[(1*R*,4*S*,5*R*)-5-((*E*)-4-Benzo[b]thiophen-2-yl-3-hydroxy-but-1-enyl)-4-hydroxy-3,3-dimethyl-2-oxo-cyclopentyl]-hept-5-enoic acid (2-hydroxy-ethyl)-amide (**64,65**)

(3*S*,4*R*,5*R*)-4-((*E*)-4-Benzo[b]thiophen-2-yl-3-hydroxy-but-1-enyl)-3-hydroxy-2,2-dimethyl-5-[(Z)-6-(1–H-tetrazol-5-yl)-hex-2-enyl]-cyclopentanone (**66,67**)

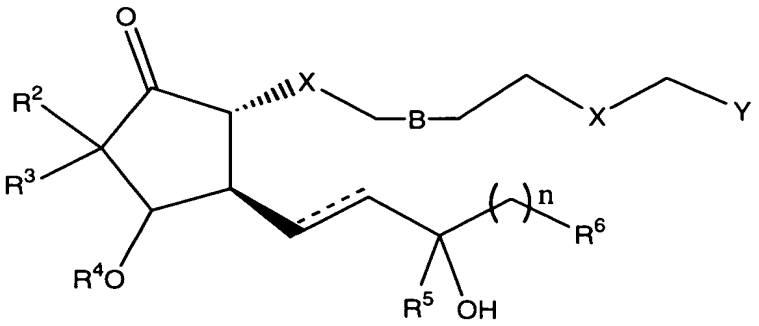
(*Z*)-7-[(1*R*,4*S*,5*R*)-5-((*E*)-4-Benzo[*b*]thiophen-2-yl-3-hydroxy-but-1-enyl)-4-hydroxy-3,3-dimethyl-2-oxo-cyclopentyl]-hept-5-enoic acid amide (**68,69**)

(*Z*)-7-[(1*R*,4*S*,5*R*)-5-((*E*)-4-Benzo[*b*]thiophen-2-yl-3-hydroxy-but-1-enyl)-4-hydroxy-3,3-dimethyl-2-oxo-cyclopentyl]-hept-5-enoic acid methyl ester (**70,71**)

7-[(1*R*,4*S*,5*R*)-5-((*E*)-4-Benzo[*b*]thiophen-2-yl-3-hydroxy-but-1-enyl)-4-hydroxy-3,3-dimethyl-2-oxo-cyclopentyl]-hept-5-ynoic acid methyl ester (**72,73**)

7-[(1*R*,4*S*,5*R*)-5-((*E*)-4-Benzo[*b*]thiophen-2-yl-3-hydroxy-but-1-enyl)-4-hydroxy-3,3-dimethyl-2-oxo-cyclopentyl]-hept-5-ynoic acid (**74,75**).

3. A compound represented by Formula I:



Formula I

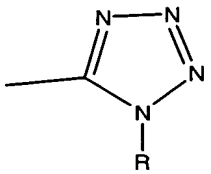
wherein the dashed lines indicate the presence or absence of a bond, the hatched wedges indicate the α (down) configuration, and the solid triangles indicate the β (up) configuration;

B is a single, double, or triple covalent bond;

n is 0-6;

X is CH_2, S or O;

Y is any pharmaceutically acceptable salt of CO_2H, or CO_2R, $CONR_2$, $CONHCH_2CH_2OH$, $CON(CH_2CH_2OH)_2$, CH_2OR, $P(O)(OR)_2$, $CONRSO_2R$, $SONR_2$, or



R is H, C_{1-6} alkyl or C_{2-6} alkenyl;

R^2 and R^3 are C_{1-6} linear alkyl which may be the same or different, and may be bonded to each other such that they form a ring incorporating the carbon to which they are commonly attached;

R^4 is hydrogen, R, C(=O)R, or any group that is easily removed under physiological conditions such that R^4 is effectively hydrogen;

R^5 is hydrogen or R;

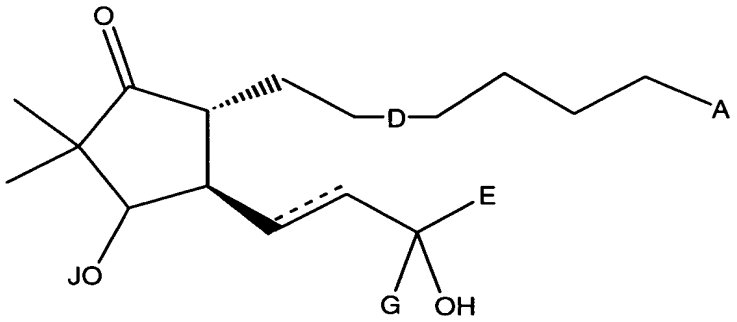
R^6 is

i) hydrogen;

ii) a linear or branched hydrocarbon containing between 1 and 8 carbon atoms, which may contain one or more double or triple bonds, or oxygen or halogen derivatives of said hydrocarbon, wherein 1-3 carbon or hydrogen atoms may be substituted by O or a halogen; or

iii) aryloxy, heteroaryloxy, C_{3-8} cycloalkyloxy, C_{3-8} cycloalkyl, C_{6-10} aryl or C_{3-10} heteroaryl, wherein one or more carbons is substituted with N, O, or S; and which may contain one or more substituents selected from the group consisting of halogen, trihalomethyl, cyano, nitro, amino, hydroxy, C_{6-10} aryl, C_{3-10} heteroaryl, aryloxy, heteroaryloxy, C_{1-6} alkyl, OR, SR, and SO_2R; and

the compound of Formula I is not a compound of Formula II



Formula II

wherein A is CO_2H, CO_2Me, or CO_2Et;

D is a single, double, or triple covalent bond;

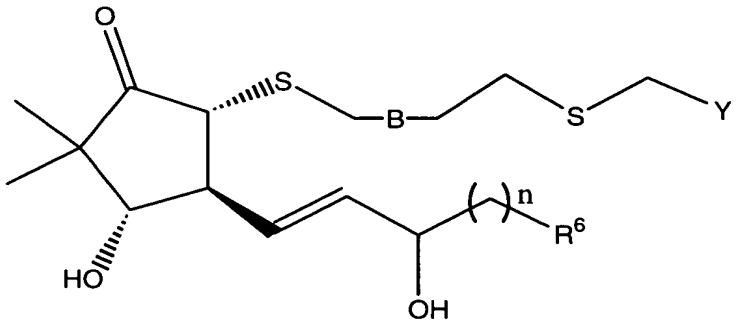
E is a linear, branched, or cycloalkyl chain of 3 to 7 carbons, trifluoromethylbutyl, hydroxylalkyl, or CH_2R^7 wherein R^7 is phenyl, cyclopentyl, phenoxy, chlorophenoxy, propoxy, or $-CH_2SCH_2CH_3$;

J is hydrogen, R, C(=O)R, or any group that is easily removed under physiological conditions such that R^4 is effectively hydrogen; and

G is H or CH_3.

4. The compound of claim 18 wherein A is CO_2R^8, wherein R^8 is any linear, branched, or cyclic alkyl group having from 3 to 6 carbons.

5. The compound of claim 18 which is further represented by Formula III



Formula III

wherein Y is CO_2R, or any pharmaceutically acceptable salt of CO_2H.

6. The compound of claim 19 wherein R^6 is C_{6-10} aryl or C_{3-10} heteroaryl, wherein one or more carbons is substituted with N, O, or S; and which may contain one or more substituents selected from the group consisting of halogen, trihalomethyl, cyano, nitro, amino, hydroxy, C_{1-6} alkyl, OR, SR, and SO_2R.

7. The compound of claim 20 wherein R^6 is napthyl, benzofuranyl, or benzothienyl, which may contain one or more substituents selected from the group consisting of halogen, trihalomethyl, cyano, nitro, amino, hydroxy, C_{1-6} alkyl, OR, SR, and SO_2R.

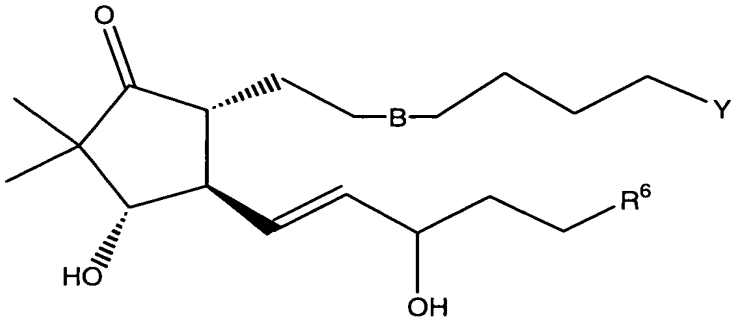
8. The compound of claim 21 wherein Y is CO_2H or CO_2Me.

9. The compound of claim 22 where R^6 is 3-chlorobenzothien-2-yl.

10. The compound of claim 23 where n is 2.

11. The compound of claim 24 where B is a single bond.

12. The compound of claim 18 which is further represented by Formula IV



Formula IV

wherein Y is CO_2R or any pharmaceutically acceptable salt of CO_2H; and

R^6 is C_{6-10} aryl or C_{3-10} heteroaryl, wherein one or more carbons is substituted with N, O, or S; and which may contain one or more substituents selected from the group consisting of halogen, trihalomethyl, cyano, nitro, amino, hydroxy, C_{1-6} alkyl, OR, SR, and SO_2R.

13. The compound of claim 26 wherein Y is CO_2H or CO_2Me.

14. The compound of claim 27 wherein R^6 is phenyl.

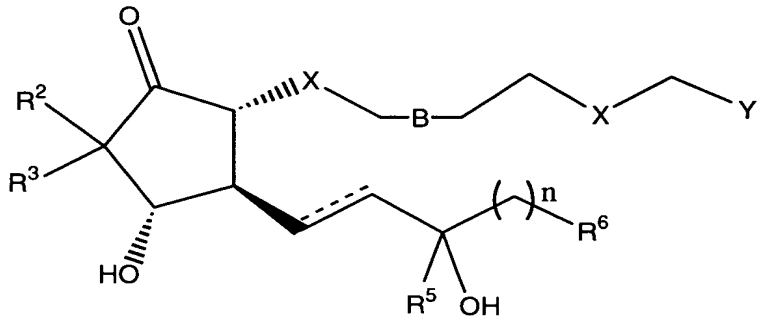
15. The compound of claim 28 wherein B is a double bond.

16. The compound of claim 27 wherein R^6 is napthyl, benzofuranyl, or benzothienyl, which may contain one or more substituents selected from the group consisting of halogen, trihalomethyl, cyano, nitro, amino, hydroxy, C_{1-6} alkyl, OR, SR, and SO_2R.

17. The compound of claim 30 wherein R^6 is 3-chlorobenzothien-2-yl.

18. The compound of claim 31 wherein B is a double or triple bond.

19. The compound of claim 18 which is further represented by Formula V



Formula V

wherein at least one of R^2 and R^3 is not methyl.

20. The compound of claim 33 wherein R^2 and R^3 have a total number of carbon atoms of 6 or less.

21. The compound of claim 34 wherein R^5 is hydrogen.

22. The compound of claim 18 wherein said compound is selected from the group consisting of (3-{(1*R*,4*S*,5*S*)-5-(3-chloro-benzo[b]thiophen-2-yl)-3-hydroxy-pent-1-enyl]-4-hydroxy-3,3-dimethyl-2-oxo-cyclopentylsulfanyl}-propylsulfanyl)-acetic acid methyl ester (**21, 22**);

(3-{(1*R*,4*S*,5*S*)-5-(3-chloro-benzo[b]thiophen-2-yl)-3-hydroxy-pent-1-enyl]-4-hydroxy-3,3-dimethyl-2-oxo-cyclopentylsulfanyl}-propylsulfanyl)-acetic acid (**23, 24**);

(*Z*)-7-{(1*R*,4*S*,5*R*)-5-[(*E*)-5-(3-chloro-benzo[b]thiophene-2-yl)-3-hydroxy-pent-1-enyl]-4-hydroxy-3,3-dimethyl-2-oxo-cyclopentyl}-hept-5-ynoic acid methyl ester (**34, 35**);

(*Z*)-7-{(1*R*,4*S*,5*R*)-5-[(*E*)-5-(3-chloro-benzo[b]thiophene-2-yl)-3-hydroxy-pent-1-enyl]-4-hydroxy-3,3-dimethyl-2-oxo-cyclopentyl}-hept-5-ynoic acid (**36,37**);

(*Z*)-7-{(1*R*,4*S*,5*R*)-5-[(*E*)-5-(3-chloro-benzo[b]thiophene-2-yl)-3-hydroxy-pent-1-enyl]-4-hydroxy-3,3-dimethyl-2-oxo-cyclopentyl}-hept-5-enoic acid methyl ester (**38,39**);

(*Z*)-7-{(1*R*,4*S*,5*R*)-5-[(*E*)-5-(3-chloro-benzo[b]thiophene-2-yl)-3-hydroxy-pent-1-enyl]-4-hydroxy-3,3-dimethyl-2-oxo-cyclopentyl}-hept-5-enoic acid (**40,41**);

(Z)-7-[(1R,4S,5R)-4-Hydroxy-5-((E)-3-hydroxy-5-phenyl-pent-1-enyl)-3,3-dimethyl-2-oxo-cyclopentyl]-hept-5-enoic acid methyl ester (**50,51**)

(Z)-7-[(1R,4S,5R)-4-Hydroxy-5-((E)-3-hydroxy-5-phenyl-pent-1-enyl)-3,3-dimethyl-2-oxo-cyclopentyl]-hept-5-enoic acid (**52,53**)

(*Z*)-7-[(1*R*,4*S*,5*R*)-5-((*E*)-4-Benzo[b]thiophen-2-yl-3-hydroxy-but-1-enyl)-4-hydroxy-3,3-dimethyl-2-oxo-cyclopentyl]-hept-5-enoic acid (**54,55**)

7-[(1*R*,4*S*,5*R*)-5-((*E*)-4-Benzo[b]thiophen-2-yl-3-hydroxy-but-1-enyl)-4-hydroxy-3,3-dimethyl-2-oxo-cyclopentyl]-heptanoic acid (**56,57**)

(*Z*)-7-[(1*R*,4*S*,5*R*)-5-(4-Benzo[b]thiophen-2-yl-3-hydroxy-butyl)-4-hydroxy-3,3-dimethyl-2-oxo-cyclopentyl]-hept-5-enoic acid (**58,59**)

(*Z*)-7-[(1*R*,4*S*,5*R*)-5-((*E*)-4-Benzo[b]thiophen-2-yl-3-hydroxy-but-1-enyl)-4-hydroxy-3,3-dimethyl-2-oxo-cyclopentyl]-hept-5-enoic acid ethylamide (**60,61**)

(*Z*)-7-[(1*R*,4*S*,5*R*)-5-((*E*)-4-Benzo[b]thiophen-2-yl-3-hydroxy-but-1-enyl)-4-hydroxy-3,3-dimethyl-2-oxo-cyclopentyl]-hept-5-enoic acid diethylamide (**62,63**)

(*Z*)-7-[(1*R*,4*S*,5*R*)-5-((*E*)-4-Benzo[b]thiophen-2-yl-3-hydroxy-but-1-enyl)-4-hydroxy-3,3-dimethyl-2-oxo-cyclopentyl]-hept-5-enoic acid (2-hydroxy-ethyl)-amide (**64,65**)

(3*S*,4*R*,5*R*)-4-((*E*)-4-Benzo[b]thiophen-2-yl-3-hydroxy-but-1-enyl)-3-hydroxy-2,2-dimethyl-5-[(Z)-6-(1–H-tetrazol-5-yl)-hex-2-enyl]-cyclopentanone (**66,67**)

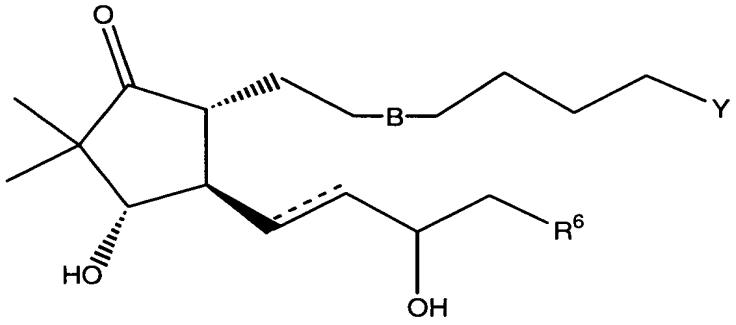
(*Z*)-7-[(1*R*,4*S*,5*R*)-5-((*E*)-4-Benzo[*b*]thiophen-2-yl-3-hydroxy-but-1-enyl)-4-hydroxy-3,3-dimethyl-2-oxo-cyclopentyl]-hept-5-enoic acid amide (**68,69**)

(*Z*)-7-[(1*R*,4*S*,5*R*)-5-((*E*)-4-Benzo[*b*]thiophen-2-yl-3-hydroxy-but-1-enyl)-4-hydroxy-3,3-dimethyl-2-oxo-cyclopentyl]-hept-5-enoic acid methyl ester (**70,71**)

7-[(1*R*,4*S*,5*R*)-5-((*E*)-4-Benzo[*b*]thiophen-2-yl-3-hydroxy-but-1-enyl)-4-hydroxy-3,3-dimethyl-2-oxo-cyclopentyl]-hept-5-ynoic acid methyl ester (**72,73**)

7-[(1*R*,4*S*,5*R*)-5-((*E*)-4-Benzo[*b*]thiophen-2-yl-3-hydroxy-but-1-enyl)-4-hydroxy-3,3-dimethyl-2-oxo-cyclopentyl]-hept-5-ynoic acid (**74,75**).

23. The compound of claim 18 which is further represented by Formula XIII



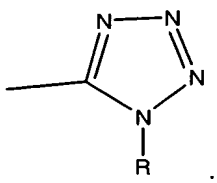
Formula XIII

wherein B represents a single or double bond;

and R^6 is napthyl, benzofuranyl, or benzothienyl, which may contain one or more substituents selected from the group consisting of halogen, trihalomethyl, cyano, nitro, amino, hydroxy, C_{1-6} alkyl, OR, SR, and SO_2R.

24. The compound of claim 47 wherein R^6 is benzothien-2-yl.

25. The compound of claim 48 wherein Y is any pharmaceutically acceptable salt of CO_2H, or CO_2R, $CONR_2$, $CONHCH_2CH_2OH$, $CON(CH_2CH_2OH)_2$, or



26. The compound of claim 49 wherein the dashed line indicates the presence of a bond and B is a double bond.

27. The compound of claim 49 wherein the dashed line indicates the presence of a bond and B is a single bond.

28. The compound of claim 49 wherein the dashed line indicates the absence of a bond and B is a double bond.